UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

IN RE: VALSARTAN, LOSARTAN, AND IRBESARTAN PRODUCTS LIABILITY LITIGATION	**MDL No. 2875**
THIS DOCUMENT RELATES TO ALL CASES	**HON. ROBERT B. KUGLER** **CIVIL NO. 19-2875 (RBK)(KMW)**

PLAINTIFFS' *DAUBERT* MOTION TO EXCLUDE CLASS CERTIFICATION OPINIONS OF ERIC SHEININ, PH.D.

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I. INTRODUCTION

Dr. Eric Sheinin is a former employee of the U.S. Food and Drug Administration ("FDA") and of the United States Pharmacopeia ("USP"). Dr. Sheinin submitted an expert report that the Mylan Defendants claim relates to "class certification issues" and "rebut[s] the class certification opinions" of Plaintiffs' expert Dr. Ron Najafi. However, Dr. Sheinin testified that he had no familiarity with what class certification means, and his opinions in no way undermine (let alone, address) any of the assertions in Plaintiffs' Motion for Class Certification. (Sheinin Dep. 57:9-16 (**Ex. 1**).)

Having never looked at Mylan's Drug Master File ("DMF") (nor any other internal company documents or deposition testimony despite listing such materials in his Report), Dr. Sheinin opines that Mylan's adulterated and misbranded VCDs met both Mylan's DMF specification and USP specification. Dr. Sheinin also disagrees with the opinions of Dr. Ron Najafi, and asserts that Mylan's NDMA/NDEA contaminated VCDs "would be considered the same as … the RLD." (Sheinin Report, ¶ 99 (**Ex. 2**).) In coming to these opinions, Dr. Sheinin relies on a combination of willful blindness, complete disregard for undisputed facts, and application of an inappropriate methodology to guide his analysis, including resting on the incorrect assumption that NDMA/NDEA are not genotoxic impurities.

II. APPLICABLE LAW

A. *Daubert* Standard

The admissibility of expert testimony is determined pursuant to Federal Rule of Evidence 702. The party offering the proposed expert testimony bears the burden of establishing the admissibility of the testimony by a preponderance of the evidence. *Padillas v. Stork-Gamco, Inc.,* 186 F.3d 412, 417-18 (3d Cir. 1999).

First, Rule 702 "requires the witness to have 'specialized knowledge' regarding the area of

testimony" proffered by the witness. *Waldorf v. Shuta*, 142 F.3d 601 (3d Cir 1998). Once qualified, an "expert's opinions must be based on the methods and procedures of science, rather than on subjective belief or unsupported speculation." *In re Paoli R.R. Yard PCB Litigation*, 35 F.3d 717, 742 (3d Cir. 1994) (citations and internal quotations omitted). Thus, "the expert must have 'good grounds' for his or her belief." *Id.* (quoting *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579, 590 (1993)). These good grounds must support each step of the analysis and, "*any* step that renders the analysis unreliable under the *Daubert* factors renders the expert's testimony inadmissible." *Id.* at 745. Judges within this Circuit also consider how and when the methodology is used outside of litigation. *Paoli*, 35 F.3d at 742 (discussing reliability factors under *Daubert* and Third Circuit case law).

Importantly, the Third Circuit has held that "[i]t is an abuse of discretion to admit expert testimony which is based on assumptions lacking any factual foundation in the record." *Steyck v. Bell Helicopter Textron, Inc.*, 295 F.3d 408, 414 (3d Cir. 2002) (citing *Elcock v. Kmart Corp.*, 233 F.3d 734, 756 & n.13 (3d Cir. 2000)). Expert testimony that is contrary to law or fact, or that seeks to misstate the applicable law to the jury, is unhelpful. *See, e.g.*, *SEC v. Ambassador Advisors, LLC*, -- F. Supp. 3d –, *5 (E.D. Pa. Dec. 21, 2021) (**Ex. 8**). Expert analysis also must have sufficient support in facts or data for the conclusions reached. *See, e.g.*, *Mondis Tech. Ltd. v. LG Elecs., Inc.*, No. 15-4431, 2021 WL 4077563, at *3 (D.N.J. Sept. 8, 2021) (**Ex. 7**). Opinions that rest on "assumptions and conclusions that are not supported by the factual record" have been excluded on the basis that it would not "aid the jury in resolving a factual dispute" because it does not "fit under the facts of the case." *Meadows*, 306 F. App'x at 790 (citing *Stecyk*, 295 F.3d at 414, and quoting *Lauria*, 145 F.3d at 599).

Furthermore, "*Daubert*'s gatekeeping requirement .... make[s] certain that an expert, whether basing testimony upon professional studies or personal experience, employs in the courtroom the same level of intellectual rigor that characterizes the practice of an expert in the relevant field.'" *Elcock v. Kmart Corp.*, 233 F.3d 734, 746 (3d Cir. 2000) (quoting *Kumho Tire Co. v. Carmichael*, 526 U.S. 137, 152 (1999)); *see also Magistrini v. One Hour Martinizing Dry Cleaning*, 180 F.Supp.2d 584, 594 (D.N.J.2002*), aff'd,* 68 Fed. Appx. 356 (3d Cir. 2003).

III. ARGUMENT

A. Dr. Sheinin's Opinions that Mylan's Valsartan API Met DMF Specification or USP Specification is Premised on No Reliable Methodology, Fails to Address Plaintiffs' Claims, and Has No Bearing on Class Certification

Dr. Sheinin ultimately fails to apply an acceptable methodology, as he failed to review key source documents he supposedly "relied on" in forming his opinions, and failed to apply established facts and applicable regulations. Instead, Dr. Sheinin resorted to making up his own set of facts on which to base his opinions. As this Court has recognized (including through its detailed set of opinions on Defendants' Motion to Dismiss), Plaintiffs' claims against the Manufacturer Defendants, including Mylan, rest on the allegations that Defendants sold VCDs in violation of state and federal law, and that were adulterated and misbranded, and contaminated with the potent carcinogens NDMA and NDEA, which contamination and the failure to detect or prevent it stemmed from egregious violations of current good manufacturing practices ("cGMPs"). The sale of Mylan's VCDs, therefore, should not have occurred and Plaintiffs and Class Members suffered economic losses by purchasing these economically worthless products that never should have entered the stream of commerce in the United States.

Mylan does not dispute that every single batch of its VCDs sold in the United States contained NDMA and/or NDEA, and indeed, ***Mylan itself recalled every single batch*** of its VCDs within expiry. The FDA expressly told Mylan in a Warning Letter (that remains unresolved to this

date) that it observed "significant deviations from [CMGPs]" related to the manufacture of Mylan's Valsartan API, and, ultimately, that Mylan's Valsartan API was "adulterated within the meaning of [21 U.S.C. § 351]" and thereby illegal to distribute in the United States per 21 U.S.C. § 331(a). (Sheinin Dep. Ex. 3, at 1 (**Ex. 3**).)

Those facts do not change whether or not Mylan's Valsartan API technically met its DMF specification or USP specification (which it did not, *infra*). Dr. Sheinin expressly disavowed making any determination: (a) regarding the "quality of" or the "adequacy of" Mylan's DMF (Sheinin Dep. 52:22-54:2; 171:18-172:7); or (b) that Mylan was any time in compliance with cGMPs (Sheinin Dep. 54:20-55:5; 66:1-67:4; 74:19-75:5.) And Mylan itself has offered no other experts on those points.

Completely divorced from actual issues in the case is Dr. Sheinin's primary opinion that Mylan's valsartan API nevertheless *technically* met its DMF specification and USP specification because Mylan's failure to identify NDEA as a potential impurity led to there being no required testing or specification for NDEA in either specification. As wrongheaded as this opinion is (discussed *infra*), it is also completely irrelevant and unhelpful to the jury or Court to resolve any disputed issue. The indisputable facts remain and are unaffected by Dr. Sheinin's opinions: Mylan's VCDs were contaminated with potent carcinogens throughout the class period; were unquestionably adulterated and misbranded pursuant to federal law (as evidenced both by official FDA determinations and Mylan's recall decisions); and were unlawfully sold to Plaintiffs and Class Members. Put simply, Dr. Sheinin's misleading opinions relating to Mylan's valsartan API meeting DMF and/or USP specification are irrelevant. *In re Paoli R.R. Yard PCB Litig.*, 35 F.3d at 742-43 ("In addition to reliability, Rule 702 requires that the expert's testimony must assist the trier of fact.").

B. Dr. Sheinin's Opinion that Mylan's VCDs Met their DMF and USP Specification is Unreliable

After providing a lengthy discussion of DMFs and USP Monographs, Dr. Sheinin concludes in his report that "Mylan's Valsartan USP API continued to meet its specification as well as its DMF specification" for the entirety of the time Mylan was distributing NDMA/NDEA contaminated, adulterated, and misbranded VCDs onto the U.S. market. (Sheinin Report ¶ 68.)

1. Dr. Sheinin Did Not Review the DMF and Thus Cannot Reliably Opine that Mylan's VCDs Did Meet the DMF Specification

Dr. Sheinin comes to this conclusion despite having done no predicate work that would be required for such an opinion to be admissible under Rule 702, a fact that renders his testimony inadmissible net opinions. *May v. Atlantic City Hilton*, 128 F. Supp. 195, 198 (D.N.J. 2000) ("The net opinion rule is that an expert's bare conclusions, unsupported by factual evidence, are inadmissible."). For one, Dr. Sheinin "didn't review any part of the drug master file" and "never saw the drug master file." (Sheinin Dep. 51:12-15; 54:1-2.) Dr. Sheinin testified further that he only "glanced at one of the ANDAs" but that it contained "very little information" and mostly "made reference to the drug master file" which he did not review. (Sheinin Dep. 51:18-52:17.) In short, Dr. Sheinin's assertion that Mylan's VCDs met their DMF specification is based on "subjective belief [and] unsupported speculation." *In re Paoli R.R. Yard PCB Litigation*, 35 F.3d at 742.

Mylan and Dr. Sheinin may counter that Dr. Sheinin was only opining as to Mylan's VCDs meeting the DMF *specification*. However, as Dr. Sheinin himself agreed, the DMF specification is an output of all of the work that is done in the DMF, and is not an independent document that is simply created from whole cloth. (Sheinin Dep. 174:18-176:20.) The distinction is especially important when, as Dr. Sheinin does, one attempts to draw inferences from the *absence of* certain tests (i.e., NDMA/NDEA tests) in the DMF specification. Specifically, Dr. Sheinin rests his entire

premise on the absence of specific tests for NDMA/NDEA, surmising that they would be treated as "any other [***non-genotoxic***] impurity" with a limit of 0.1% (or 1,000 parts per million). (Sheinin Dep. 281:2-282:2.) The fallacy of this false assertion, from both a factual and regulatory standpoint, is discussed *infra*.

Had Dr. Sheinin reviewed the DMF, he would have seen that Mylan certified [redacted]. (Sheinin Dep. 176:21-181:13; Sheinin Dep. Ex. 10, at 80-82 (**Ex. 9**) ([redacted]).) Dr. Sheinin was completely unaware of these DMF certifications. (Sheinin Dep. 181:8-13.)

Expert analysis also must have sufficient support in facts or data for the conclusions reached. *See, e.g.*, *Mondis*, 2021 WL 4077563, at *3 (**Ex. 7**). Dr. Sheinin's complete failure to consider how Mylan's certification [redacted], in interpreting the absence of such tests in DMF specification to reach his conclusion that they would be treated as "any other [non-genotoxic] impurity," is completely contrary to facts in the record and lacking in support. This is a classic net opinion.

*2. **Dr. Sheinin Pretends that NDMA/NDEA Are Not Genotoxic Impurities***

No one in this case disputes that NDMA/NDEA are regarded as genotoxic impurities for purposes of FDA regulations. The specific regulation governing genotoxic impurities is ICH M7, which itself states that it is applicable to "those impurities that are DNA reactive."[1] (Sheinin Dep.

[1] Although the FDA ICH M7 was adopted in March 2018, substantially identical versions have existed and been applicable to Defendants here for years, [redacted].

Ex. 5 – ICH M7 (**Ex. 4**).) That guidance explicitly states that that "N-nitroso-" compounds (including NDMA and NDEA) are within its purview, and specifically identifies these compounds as belonging to the "Cohort of Concern," a "group of high potency mutagenic carcinogens" of "such high potency" that special AIs/TTCs would have to be developed. (**Ex. 4**, at 5.)

Dr. Sheinin never reviewed ICH M7. (Sheinin Dep. 82:16-23.) He simply pretends that NDMA/NDEA are not genotoxic impurities (Sheinin Dep. 281:2-282:2), and treats them as such, thus arriving at his unsupported determination that NDMA/NDEA were acceptable at levels below 1,000 parts per million. *Not even the Defendants themselves have taken this position in the litigation*.

The absurdity of Dr. Sheinin's opinion can be explained in part by looking at the outcome of the FDA's AI/TTC approach to NDMA/NDEA, which was explicitly done pursuant to ICH M7. For NDEA in Mylan's VCDs, for example, the ultimate AI/TTC at which the FDA arrived was 0.083 parts per million (~12,000 times less than Dr. Sheinin's result!).[2]

Furthermore, had Dr. Sheinin actually reviewed any of the internal documents or testimony provided to him by counsel (his testimony was that he reviewed none of it (Sheinin Dep. 206:9-20)), he may have learned that the FDA's position *expressly articulated to Mylan* in *a DMF deficiency letter* was:

[redacted]

(Sheinin Dep. 101:2-108:6; Sheinin Ex. 7 – FDA DMF Deficiency Letter March 14, 2019, at 5 (**Ex. 5**) (emphasis added).)

[2] *See* https://www.fda.gov/media/141720/download.

Expert testimony that is contrary to law or fact, or that seeks to misstate the applicable law to the jury, is unhelpful. *See, e.g.*, *SEC v. Ambassador Advisors, LLC*, -- F. Supp. 3d –, *5 (E.D. Pa. Dec. 21, 2021) (**Ex. 8**). Dr. Sheinin's make believe that NDMA/NDEA are treated as non-genotoxic impurities under FDA regulations (a position no Defendant in this case has even dared stake out) when that is clearly untrue, renders his opinions unreliable and unhelpful to the jury, apart from being net opinions.

3. Dr. Sheinin Concedes that Mylan Had a Responsibility to Evaluate its Manufacturing Process for Genotoxic Impurities and Propose Appropriate Testing Criteria in its DMF and/or USP Specification

Dr. Sheinin conceded that manufacturers including Mylan "[are] also responsible for evaluating the process chemistry to predict potential impurities that may arise from the chemical reactions that take place[.]" (Sheinin Dep. 133:17-134:8.). This is the necessary predicate to establishing what to test for and the specification levels if some level of a potential impurity is acceptable. Thus, the absence of NDMA/NDEA testing in Mylan's DMF and/or USP specifications is actually on account of Mylan's very failures at issue in this litigation, including but not limited to significant cGMP failures, that resulted in NDMA/NDEA contamination and adulteration of Mylan's VCDs.

For example, instead of certifying in the DMF that there was no possibility of genotoxic impurity formation (as discussed *supra*), Mylan was required to perform fulsome and adequate risk assessment (as required to fulfill its cGMP obligations) and, had it Mylan done so, it would have easily determined there was a risk of NDEA creation based on its manufacturing process. Indeed, the FDA told Mylan in its Warning Letter that Mylan's principal shortcoming regarding its VCDs was its failure "to anticipate the presence of NDMA or NDEA impurities based on your assessment of the API manufacturing process." (FDA Unit 8 Warning Letter (**Ex. 3**).) Had Mylan done a fulsome risk assessment and appropriately anticipated the problem, Mylan either would

have had to change its manufacturing practice so that NDEA would not form or initiate the process under ICH M7 to set AIs/TTCs (as was eventually done). The lack of NDMA/NDEA testing in the DMF specification is just symptomatic of Mylan's failures, rather than a defense to liability.

Similarly, Dr. Sheinin conceded that "if the individual [USP] monograph is inadequate to control [an] impurity, the manufacturer is responsible for developing, validating appropriate analytical procedures and communicating with USP" pursuant to what Dr. Sheinin described as the "flexible monograph approach" designed to accommodate when a particular manufacturer's process creates "a different set of impurities." (Sheinin Dep. 128:18-131:24.) Dr. Sheinin also admitted that he had seen no evidence of Mylan communicating with USP regarding Valsartan USP pursuant to this flexible monograph approach at any point. (Sheinin Dep. 129:4-10.) Once again, the absence of NDMA/NDEA testing criteria in the USP monograph is symptomatic of Mylan's failure to anticipate NDMA/NDEA in its VCDs, rather than a defense to its liability and responsibility.

C. <u>Dr. Sheinin's Critique of Dr. Najafi's Expert Declaration Unraveled at His Deposition</u>

Dr. Sheinin attacks Dr. Najafi's conclusion that NDMA- and NDEA-contaminated VCDs are not therapeutic equivalents of their respective Reference Listed Drugs ("RLDs"), in this case DIOVAN and EXFORGE.

Dr. Sheinin's position is an extension of his first opinion, namely, that if the drug substance meets acceptance criteria, then it is necessarily therapeutically equivalent. As Dr. Sheinin explained himself:

> THE WITNESS: As long as the generic or any -- any drug substance meets the acceptance criteria in the specification, then -- and that includes not only the assay but the impurity testing, then I would consider that to be the same as any other API of that same chemical that has also met the acceptance criteria in the specification.

(Sheinin Dep. 239:2-12.)

To begin, Dr. Sheinin agreed that "therapeutic equivalence" is the regulatory touchstone for determining interchangeability or substitutability of generic drugs for each other or the RLD. (Sheinin Dep. 224:16-225:21.) Dr. Sheinin then asserted that his opinion was that NDMA- and NDEA-contaminated VCDs ***are*** therapeutically equivalent to the RLDs under the Orange Book. (Sheinin Dep. 227:18-21.) This is despite the fact that Dr. Sheinin admitted that he did not even bother to look up how the FDA defines therapeutic equivalence and could not recall himself what it meant, so this is yet another net opinion. (Sheinin Dep. 228:13-229:9.) Ultimately, Dr. Sheinin attempted to explain that his own interpretation was based purely on the VCDs meeting the specification's acceptance criteria, which is clearly an inadequate basis for his opinion – and thus, as with his other opinions, based on an inadequate methodology.

Dr. Sheinin's misapplication of regulations and misrepresenting of the law, on top of conclusory opinions without review of the source documents, would be unhelpful to the jury and should be excluded. Meeting acceptance criteria is not how the FDA defines "therapeutic equivalence" for purposes of the Orange Book. The FDA defines "therapeutic equivalence" in the FDA's Orange Book preface, which Dr. Sheinin testified he had not reviewed. (Sheinin Dep. 246:22-247:2; Sheinin Dep. Ex. 14 – FDA Orange Book Preface (**Ex. 6**).) Upon being shown the FDA Orange Book definition, Dr. Sheinin disavowed his own definition and agreed that "manufacturing in compliance with [cGMP] regulations [is] a requirement that the FDA has for a drug to be considered therapeutically equivalent[,]" among other requirements applicable to Mylan's adulterated VCDs that result in them not being therapeutically equivalent (approved as safe and effective, meet applicable standards for quality, and are adequately labeled). (Sheinin Dep. 247:6-13.)

Dr. Sheinin's position truly unraveled, however, when he testified that – according to his view – a drug with an impurity guaranteed to kill anyone who ingested it would still be considered equivalent to the RLD. The following exchange demonstrates the weakness of Dr. Sheinin's methodology and resulting opinions:

> Q. Okay. Let me ask a hypothetical to you, Dr. Sheinin. The specification lists impurities of not more than .1 percent in this case, right, for valsartan? That's what the specification says, right?
> A. The specification for any other unknown impurity is point – not more than .1 percent.
> Q. Right. Let's say there was some other unknown impurity that was guaranteed to kill anyone who ingested the product at levels below .1 percent, percent mortality rate, are you saying that that would be considered the same, from a purity or quality standpoint, as the RLD?
> …
> THE WITNESS: That's a very hypothetical question that has no place in the real world. But in the specification, if it's -- if it's -- has -- if it meets the specification, then it's the same.

(Sheinin Dep. 239:14-240:17.)

Thus, Dr. Sheinin believes that a drug substance with impurities guaranteed to end a human life is still somehow the therapeutic equivalent of the RLD, despite common sense and the plain wording of the FDA's definition of therapeutic equivalence. The Court should exclude this patently unreliable expert opinion.

IV. CONCLUSION

For the foregoing reasons, Dr. Sheinin should be excluded from offering his opinions.

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Respectfully submitted,

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CERTIFICATE OF SERVICE

I hereby certify that on May 3, 2022, a true and correct redacted copy of the foregoing was filed and served via the Court's CM/ECF system, and an undredacted version was served on the court and the Defense Executive Committee via email.

/s/ David J. Stanoch
David J. Stanoch